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     FILE 'REGISTRY' ENTERED AT 16:47:32 ON 23 JUN 2008
L1              STRUCTURE UPLOADED
L2            0 S L1
L3              STRUCTURE UPLOADED
L4            5 S L3
L5          125 F L3 SSS FULL

     FILE 'CAPLUS' ENTERED AT 16:50:02 ON 23 JUN 2008
L6           11 S L5

     FILE 'REGISTRY' ENTERED AT 17:08:00 ON 23 JUN 2008
L7              STRUCTURE UPLOADED
L8           11 S L7
L9          209 S L7 SSS FULL

     FILE 'CAPLUS' ENTERED AT 17:08:36 ON 23 JUN 2008
L10           3 S L9
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=> file registry
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

FILE 'REGISTRY' ENTERED AT 16:47:32 ON 23 JUN 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   22 JUN 2008  HIGHEST RN 1029806-10-7
DICTIONARY FILE UPDATES:  22 JUN 2008  HIGHEST RN 1029806-10-7

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\STNEXP\Queries\10520962generic.str
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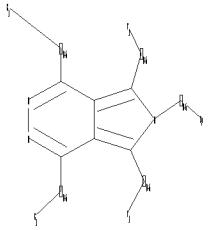

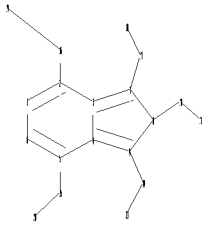

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10 11 14 15 16 17 18 19 20 21
ring nodes :
1 2 3 4 5 6 7 8 9
chain bonds :
2-16 5-15 7-17 8-10 9-14 10-11 14-21 15-20 16-19 17-18
ring bonds :
1-2 1-6 2-3 3-4 3-7 4-5 4-9 5-6 7-8 8-9
exact/norm bonds :
1-2 1-6 2-3 3-4 3-7 4-5 4-9 5-6 7-8 8-9 8-10 10-11 14-21 15-20 16-19
17-18
exact bonds :
2-16 5-15 7-17 9-14

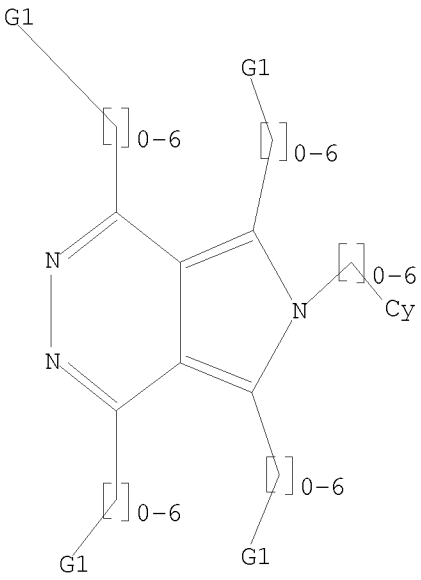
G1:H,Cy

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS

11:Atom 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS 19:CLASS 20:CLASS
21:CLASS

L1   STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1   STR



G1 H,Cy

Structure attributes must be viewed using STN Express query preparation.

=> s l1
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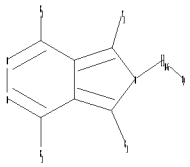
SAMPLE SCREEN SEARCH COMPLETED -   94453 TO ITERATE

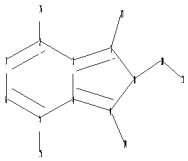
  2.1% PROCESSED   2000 ITERATIONS   0 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **INCOMPLETE**
                        BATCH   **INCOMPLETE**
PROJECTED ITERATIONS: 1870802 TO 1907318
PROJECTED ANSWERS: 0 TO   0

L2   0 SEA SSS SAM L1

=>
Uploading C:\Program Files\STNEXP\Queries\10520962simple.str





chain nodes :
10 11 14 15 16 17
ring nodes :
1 2 3 4 5 6 7 8 9
chain bonds :
2-16 5-15 7-17 8-10 9-14 10-11
ring bonds :
1-2 1-6 2-3 3-4 3-7 4-5 4-9 5-6 7-8 8-9
exact/norm bonds :
1-2 1-6 2-3 2-16 3-4 3-7 4-5 4-9 5-6 5-15 7-8 7-17 8-9 8-10 9-14
10-11

G1:H,C

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
11:Atom 14:CLASS 15:CLASS 16:CLASS 17:CLASS

L3 STRUCTURE UPLOADED

=> s l3
SAMPLE SEARCH INITIATED 16:49:18 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 6814 TO ITERATE

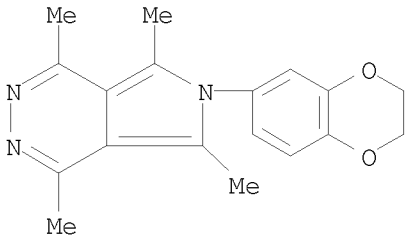
29.4% PROCESSED 2000 ITERATIONS 5 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 131331 TO 141229
PROJECTED ANSWERS: 93 TO 587

L4 5 SEA SSS SAM L3

=> d l4 scan

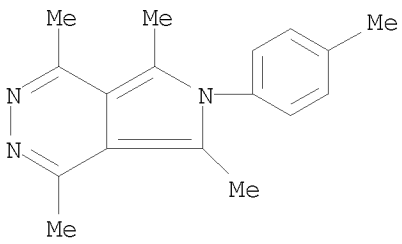
L4 5 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN 6H-Pyrrolo[3,4-d]pyridazine, 6-(2,3-dihydro-1,4-benzodioxin-6-yl)-1,4,5,7-tetramethyl-
MF C18 H19 N3 O2



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

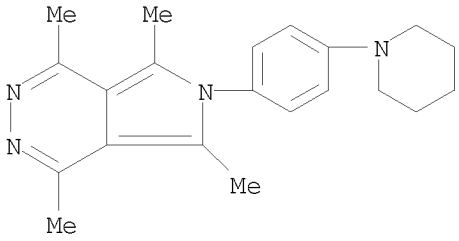
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):3

L4 5 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN 6H-Pyrrolo[3,4-d]pyridazine, 1,4,5,7-tetramethyl-6-(4-methylphenyl)-
MF C17 H19 N3



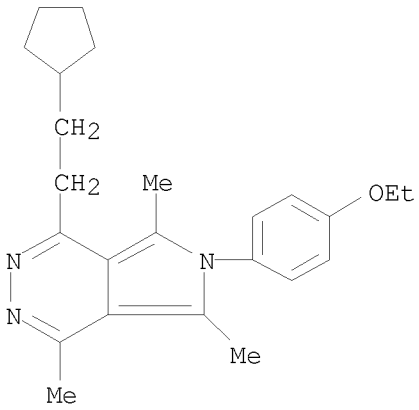
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 5 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN 6H-Pyrrolo[3,4-d]pyridazine, 1,4,5,7-tetramethyl-6-[4-(1-piperidinyl)phenyl]-
MF C21 H26 N4



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

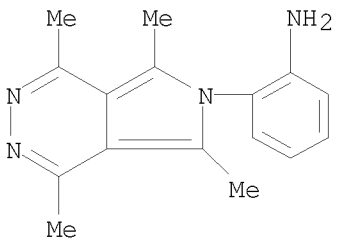
L4 5 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN 6H-Pyrrolo[3,4-d]pyridazine, 1-(2-cyclopentylethyl)-6-(4-ethoxyphenyl)-4,5,7-trimethyl-
MF C24 H31 N3 O



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L4 5 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Benzenamine, 2-(1,4,5,7-tetramethyl-6H-pyrrolo[3,4-d]pyridazin-6-yl)-
MF C16 H18 N4



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

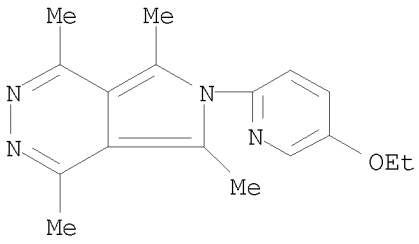
=> f l3 sss full
FULL SEARCH INITIATED 16:49:40 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 134102 TO ITERATE

100.0% PROCESSED 134102 ITERATIONS 125 ANSWERS
SEARCH TIME: 00.00.02

L5 125 SEA SSS FUL L3

=> d l5 scan

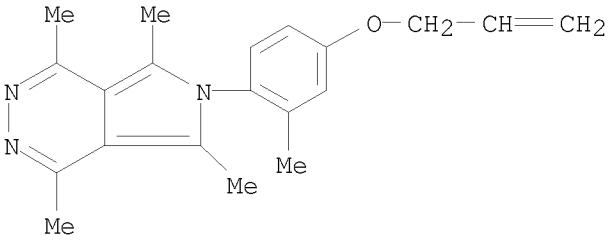
L5 125 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN 6H-Pyrrolo[3,4-d]pyridazine, 6-(5-ethoxy-2-pyridinyl)-1,4,5,7-tetramethyl-
MF C17 H20 N4 O



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

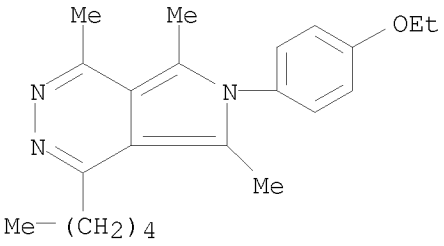
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):3

L5 125 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN 6H-Pyrrolo[3,4-d]pyridazine, 1,4,5,7-tetramethyl-6-[2-methyl-4-(2-propen-1-yloxy)phenyl]-
MF C20 H23 N3 O



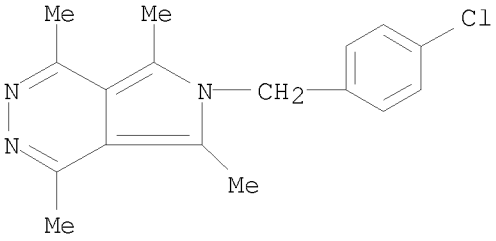
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L5 125 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN 6H-Pyrrolo[3,4-d]pyridazine, 6-(4-ethoxyphenyl)-1,5,7-trimethyl-4-pentyl-
MF C22 H29 N3 O



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L5 125 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN 6H-Pyrrolo[3,4-d]pyridazine, 6-[(4-chlorophenyl)methyl]-1,4,5,7-
tetramethyl-
MF C17 H18 Cl N3



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> file caplus
COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION
FULL ESTIMATED COST | 179.74 | 179.95

FILE 'CAPLUS' ENTERED AT 16:50:02 ON 23 JUN 2008
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FILE COVERS 1907 - 23 Jun 2008 VOL 148 ISS 26
FILE LAST UPDATED: 22 Jun 2008 (20080622/ED)

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They are available for your review at:

http://www.cas.org/legal/infopolicy.html

=> s l5
L6 11 L5

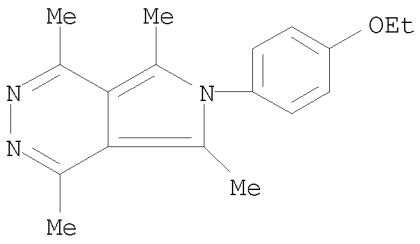
=> d l6 1-11 ti abs bib hitstr

L6 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
TI Expedited SAR study of high-affinity ligands to the α2δ subunit of voltage-gated calcium channels: Generation of a focused library using a solution-phase Sn2Ar coupling methodology
AB The SAR of the lead compound 3, a novel ligand for the α2δ subunit of voltage-gated calcium channels, was rapidly explored. Utilizing a parallel solution-phase Sn2Ar coupling approach, a focused library was obtained. The library was evaluated in vitro and afforded a series of analogs with improved potencies. The SAR trends of the library are also described.
AN 2005:1342000 CAPLUS <<LOGINID::20080623>>
DN 144:100381
TI Expedited SAR study of high-affinity ligands to the α2δ subunit of voltage-gated calcium channels: Generation of a focused library using a solution-phase Sn2Ar coupling methodology
AU Chen, Chixu; Stearns, Brian; Hu, Tao; Anker, Naomi; Santini, Angelina; Arruda, Jeannie M.; Campbell, Brian T.; Datta, Purabi; Aiyar, Jayashree; Munoz, Benitio
CS Department of Chemistry, Merck Research Laboratories, San Diego, CA, 92121, USA
SO Bioorganic & Medicinal Chemistry Letters (2006), 16(3), 746-749
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier B.V.
DT Journal
LA English
OS CASREACT 144:100381
IT 461432-09-7

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SAR of high-affinity ligands to α2δ subunit of voltage-gated calcium channels: generation of focused library using solution-phase Sn2Ar coupling methodol.)

RN 461432-09-7 CAPLUS

CN 6H-Pyrrolo[3,4-d]pyridazine, 6-(4-ethoxyphenyl)-1,4,5,7-tetramethyl- (CA INDEX NAME)

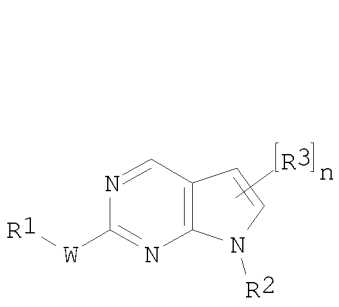


RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

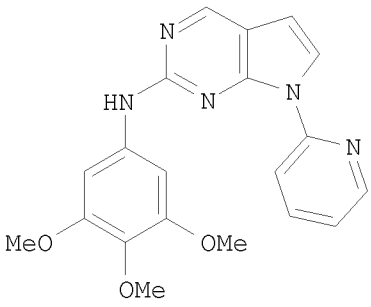
L6 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN

TI Preparation of substituted pyrrolo[2,3-d]pyrimidines as inducers of keratinocyte differentiation

GI



I



II

AB The invention provides compds. I [n = 0-2; W = NR4, S, O, SO, SO2 (wherein R4 = H, alkyl); R1 = arylalkyl, heteroarylalkyl, cycloalkylalkyl, etc.; R2 = arylalkyl, heteroarylalkyl, cycloalkylalkyl, etc.; R3 = halo, OH, XSR5, etc. (X = a bond, alkylene; R5 = H, alkyl, cycloalkylalkyl)], pharmaceutical compns. comprising such compds. and methods of using such compds. to induce undifferentiated keratinocytes to differentiate into terminally differentiated keratinocytes. The invention further provides compds. for the treatment of diseases or disorders associated with casein kinase II (CK2), TANK-binding kinase 1 (TBK1) and NIMA-related kinase 9 (NEK9). Over 200 compds. I were prepared E.g., a 4-step synthesis of II, starting from 5-bromo-2,4-dichloropyrimidine, was given.

AN 2005:1220346 CAPLUS <<LOGINID::20080623>>

DN 143:477978

TI Preparation of substituted pyrrolo[2,3-d]pyrimidines as inducers of

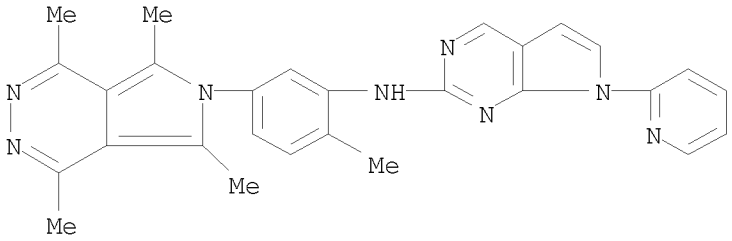
keratinocyte differentiation
IN Hong, Jiyong; Gray, Nathanael S.; Schultz, Peter
PA IRM LLC, Bermuda
SO PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005107760	A1	20051117	WO 2005-US15118	20050429

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2004-567346P P 20040430
OS CASREACT 143:477978; MARPAT 143:477978
IT 863597-72-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted pyrrolo[2,3-d]pyrimidines as inducers of keratinocyte differentiation)
RN 863597-72-2 CAPLUS
CN 7H-Pyrrolo[2,3-d]pyrimidin-2-amine, N-[2-methyl-5-(1,4,5,7-tetramethyl-6H-pyrrolo[3,4-d]pyridazin-6-yl)phenyl]-7-(2-pyridinyl)- (CA INDEX NAME)



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
TI Preparation of pyrrolopyrimidines and their analogs as protein kinase inhibitors
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention provides a novel class of compds. I-V [n = 0-2; m = 0-3; W =

NR4, S, O, SO, SO2 (wherein R4 = H, alkyl); R1 = (un)substituted (hetero)arylakyl, (hetero)cycloalkyl; R2 = (un)substituted (hetero)arylakyl, (hetero)cycloalkyl; R3 = halo, OH, XSR5, etc. (X = a bond, alkylene; R5 = H, alkyl, cycloalkylalkyl)], pharmaceutical compns. comprising such compds. and methods of using such compds. to treat or prevent diseases or disorders associated with abnormal or deregulated kinase activity, particularly diseases or disorders that involve abnormal activation of the FAK, Abl, BCR-Abl, PDGF-R, c-Kit, NPM-ALK, Flt-3, JAK2 and c-Met kinases. Over 200 compds. I-V were prepared and characterized. The preparation of the compds. I is illustrated in examples. E.g., synthesis of I [R1 = 3,4,6-(MeO)3C6H2; R2 = 2-pyridyl; R3 = H; W = NH], starting from 5-bromo-2,4-dichloropyrimidine, was given. The compds. I-V were tested against various kinases. For example, they inhibit the enzyme activity by 50% (IC50), in a concentration of from 0.001 to 0.5 μM, especially from 0.01 to 0.1 μM.

AN 2005:962258 CAPLUS <<LOGINID::20080623>>

DN 143:266947

TI Preparation of pyrrolopyrimidines and their analogs as protein kinase inhibitors

IN Choi, Ha-Soon; Wang, Zhicheng; Gray, Nathanael Schiander; Gu, Xiang-Ju; He, Xiaohui; He, Yun; Jiang, Tao; Liu, Yi; Richmond, Wendy; Sim, Taebo; Yang, Kunyong

PA IRM LLC, Bermuda

SO PCT Int. Appl., 63 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005080393	A1	20050901	WO 2005-US4630	20050214
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2005214352	A1	20050901	AU 2005-214352	20050214
	CA 2553785	A1	20050901	CA 2005-2553785	20050214
	EP 1713806	A1	20061025	EP 2005-713510	20050214
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
	CN 1918158	A	20070221	CN 2005-80004895	20050214
	BR 2005007668	A	20070717	BR 2005-7668	20050214
	JP 2007522241	T	20070809	JP 2006-553321	20050214
	MX 2006PA09158	A	20061110	MX 2006-PA9158	20060811
	IN 2006CN02987	A	20070608	IN 2006-CN2987	20060814
	US 20070225306	A1	20070927	US 2007-589099	20070611
PRAI	US 2004-544944P	P	20040214		
	WO 2005-US4630	W	20050214		

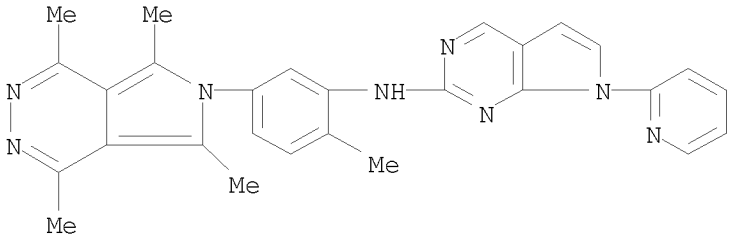
OS MARPAT 143:266947

IT 863597-72-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn of pyrrolopyrimidines and their analogs as protein kinase inhibitors)

RN 863597-72-2 CAPLUS

CN 7H-Pyrrolo[2,3-d]pyrimidin-2-amine, N-[2-methyl-5-(1,4,5,7-tetramethyl-6H-pyrrolo[3,4-d]pyridazin-6-yl)phenyl]-7-(2-pyridinyl)- (CA INDEX NAME)

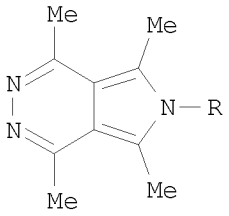


RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

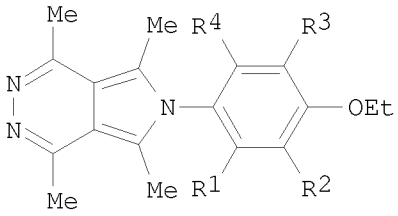
L6 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN

TI Synthesis and biological evaluation of 6-aryl-6H-pyrrolo[3,4-d]pyridazine derivatives as high-affinity ligands of the α2δ subunit of voltage-gated calcium channels

GI



I



II

AB 2H-pyrrolo[3,4-c]pyridazines I (R = 4-EtOC6H4, 2-EtO-5-pyridinyl, 5-EtO-2-pyridinyl, 5-EtO-2-pyrazinyl, 4-EtO-1-pyridazinyl, 2-EtO-5-pyrimidinyl, etc.) such as II (R1 = H, MeO, Et, H2C:CH, Me, MeS, EtO, F; R2 = H, Me; R3 = H, Me, Cl, HOCH2; R4 = H, Me) are prepared as ligands for the α2δ subunit of voltage-gated calcium channels. Ortho-substituents capable of electron-donation increase the binding of II to the α2δ subunit of voltage-gated calcium channels; electron-withdrawing substituents in the ortho-position of II decrease binding significantly. II (R1 = MeO; R2 = R3 = R4 = H) binds to the α2δ subunit of voltage-gated calcium channels from A710 cells with an IC50 value of 4 nM. Testing of tritiated ligand II (R1 = TCH2TCH; R2 = R3 = R4 = H) in purified human α2δ voltage-gated calcium channel subunits indicates that II displace Gabapentin from the α2δ subunit of voltage-gated calcium channels, and thus act as Gabapentin mimics in vitro. In the preparation of II (R1 = Et; R2 = R3 = R4 = H), a novel metal-free hydrogenation is used using hydrazine as the reductant; the reduction is effective in other systems (no data).

AN 2004:303255 CAPLUS <<LOGINID::20080623>>

DN 141:54277

TI Synthesis and biological evaluation of 6-aryl-6H-pyrrolo[3,4-d]pyridazine derivatives as high-affinity ligands of the α2δ subunit of voltage-gated calcium channels

AU Hu, Tao; Stearns, Brian A.; Campbell, Brian T.; Arruda, Jeannie M.; Chen, Chixu; Aiyar, Jayashree; Bezverkov, Robert E.; Santini, Angelina; Schaffhauser, Herve; Liu, Wensheng; Venkatraman, Shankar; Munoz, Benito

CS MRLSDB2, Department of Medicinal Chemistry, Merck Research Laboratories, San Diego, CA, 92121, USA

SO Bioorganic & Medicinal Chemistry Letters (2004), 14(9), 2031-2034
CODEN: BMCLE8; ISSN: 0960-894X

PB Elsevier Science B.V.

DT Journal

LA English

OS CASREACT 141:54277

IT 647845-61-2P 647845-62-3P 706822-55-1P
706822-56-2P 706822-57-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(heteroaryl-substituted pyrrolo[3,4-c]pyridazines are less effective ligands than aryl-substituted pyrrolo[3,4-c]pyridazines for the α2δ subunit of voltage-gated calcium channels)

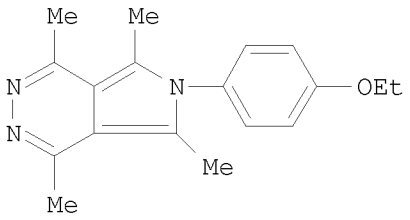
RN 647845-61-2 CAPLUS

CN 6H-Pyrrolo[3,4-d]pyridazine, 6-(6-ethoxy-3-pyridinyl)-1,4,5,7-tetramethyl- (CA INDEX NAME)

L6 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN

TI Synthesis and biological evaluation of 6-aryl-6H-pyrrolo[3,4-d]pyridazine derivatives: high-affinity ligands to the α2δ subunit of voltage gated calcium channels

GI



I

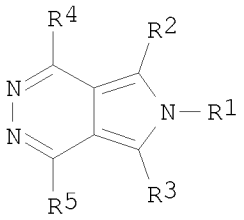
AB A novel class of 6-aryl-6H-pyrrolo[3,4-d]pyridazine ligands for the α2δ subunit of voltage-gated calcium channels has been described. Substitutions in the aryl ring of the mol. were generally not tolerated, and resulted in diminished binding to the α2δ subunit. Modifications to the pyridazine ring revealed numerous permissive substitutions, and detailed SAR studies were carried out in this portion of the mol. Replacement of the pyridazine ring Me group with an aminomethyl functionality provided greatly improved potency over the initial lead. The initial lead compound (I) displayed good rat pharmacokinetic properties, and was shown to be efficacious in the Chung model for neuropathic pain in rats.

AN 2004:153601 CAPLUS <<LOGINID::20080623>>

DN 140:357282

TI Synthesis and biological evaluation of 6-aryl-6H-pyrrolo[3,4-d]pyridazine derivatives: high-affinity ligands to the α2δ subunit of voltage gated calcium channels
AU Stearns, Brian A.; Anker, Naomi; Arruda, Jeannie M.; Campbell, Brian T.; Chen, Chixu; Cramer, Merryl; Hu, Tao; Jiang, Xiaohui; Park, Kenneth; Ren, Kun Kun; Sablad, Marciano; Santini, Angelina; Schaffhauser, Herve; Urban, Mark O.; Munoz, Benito
CS Department of Medicinal Chemistry, Merck Research Laboratories, San Diego, CA, 92121, USA
SO Bioorganic & Medicinal Chemistry Letters (2004), 14(5), 1295-1298
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science B.V.
DT Journal
LA English
OS CASREACT 140:357282
IT 461432-09-7
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); BIOL (Biological study)
(preparation of 6-aryl-6H-pyrrolo[3,4-d]pyridazine derivs. as high-affinity ligands to the α2δ subunit of voltage gated calcium channels)
RN 461432-09-7 CAPLUS
CN 6H-Pyrrolo[3,4-d]pyridazine, 6-(4-ethoxyphenyl)-1,4,5,7-tetramethyl- (CA INDEX NAME)

L6 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
TI Treatment of neuropathic pain with 6H-pyrrolo[3,4-d]pyridazine compounds
GI



I

AB The title compds. [I; R1 = (un)substituted alkyl(hetero)aryl, alkyl(hetero)cycloalkyl, (hetero)aryl, (hetero)cycloalkyl; R2-R5 = a bond, (un)substituted alkyl, alkyl(hetero)aryl, alkyl(hetero)cycloalkyl, (hetero)aryl, (hetero)cycloalkyl] were prepared as as ligands of voltage gated calcium channels (VGCC), useful in the treatment of neuropathic pain, and psychiatric and mood disorders such as, for example, schizophrenia, anxiety, depression, panic, and bipolar disorder, as well as in the treatment of pain, Parkinson s disease, cognitive dysfunction, epilepsy, circadian rhythm disorders, drug addiction, drug abuse, drug withdrawal and other. E.g., a multi-step synthesis of I [R1 = 4-EtOC6H4; R2-R4 = Me; R5 = 4-MeOC6H4] which produced a 65% effect after i.p. dosing at 30 mg/kg in spinal nerve ligation model of neuropathic pain in rats, was given. The pharmaceutical composition comprising the compound I is claimed.
AN 2004:60243 CAPLUS <<LOGINID::20080623>>
DN 140:111422
TI Treatment of neuropathic pain with 6H-pyrrolo[3,4-d]pyridazine compounds
IN Anker, Naomi Burke; Arruda, Jeannie M.; Campbell, Brian Thomas; Munoz,

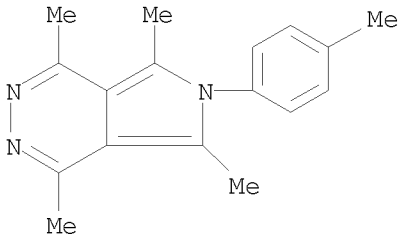
Benito; Prasit, Petpiboon; Stearns, Brian A.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 203 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004006836	A2	20040122	WO 2003-US21493	20030708
WO 2004006836	A3	20040415		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2492022	A1	20040122	CA 2003-2492022	20030708
AU 2003248907	A1	20040202	AU 2003-248907	20030708
AU 2003248907	B2	20070426		
EP 1539168	A2	20050615	EP 2003-764414	20030708
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005536507	T	20051202	JP 2004-521592	20030708
US 20060154929	A1	20060713	US 2005-520962	20051128
PRAI US 2002-394734P	P	20020711		
WO 2003-US21493	W	20030708		

OS MARPAT 140:111422
IT 647845-41-8P 647845-64-5P 647845-85-0P
647845-88-3P 647845-89-4P 647845-90-7P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 6H-pyrrolo[3,4-d]pyridazines for treating neuropathic pain)
RN 647845-41-8 CAPLUS
CN 6H-Pyrrolo[3,4-d]pyridazine-1-propanoic acid, 6-(4-ethoxyphenyl)-4,5,7-trimethyl-, methyl ester (CA INDEX NAME)

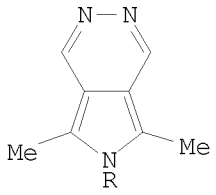
L6 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
TI Synthesis and electrophilic substitution of dipyrrolo[1,2-b:3,4-d]pyridazines
AB Dipyrrolo[1,2-b:3,4-d]pyridazines were prepared from 1,4,5,7-tetramethyl-6-R1-pyrrolo[3,4-d]-pyridazines. The dipyrrolo[1,2-b:3,4-d]pyridazines were found to have high nucleophilicity and electrophilic substitution occurs at C7, or C7 and C9 depending on the steric bulk and activity of the attacking electrophile.
AN 2003:927977 CAPLUS <<LOGINID::20080623>>
DN 140:303615
TI Synthesis and electrophilic substitution of dipyrrolo[1,2-b:3,4-d]pyridazines
AU Arsen'ev, V. G.; Arsen'eva, M. Yu.; Shopin, D. V.; Olekhnovich, L. P.
CS Rostov State University, Rostov-on-Don, 344006, Russia
SO Chemistry of Heterocyclic Compounds (New York, NY, United States)(Translation of Khimiya Geterotsiklicheskikh Soedinenii) (2003), 39(5), 669-670

CODEN: CHCCAL; ISSN: 0009-3122
PB Kluwer Academic/Consultants Bureau
DT Journal
LA English
OS CASREACT 140:303615
IT 378216-53-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of dipyrrolopyridazines from pyrrolopyridazines and their reactivity in electrophilic substitution reactions)
RN 378216-53-6 CAPLUS
CN 6H-Pyrrolo[3,4-d]pyridazine, 1,4,5,7-tetramethyl-6-(4-methylphenyl)- (CA INDEX NAME)

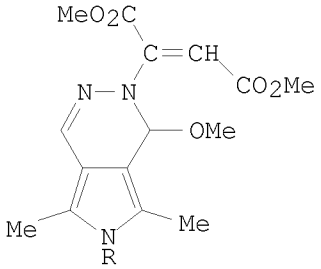


RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

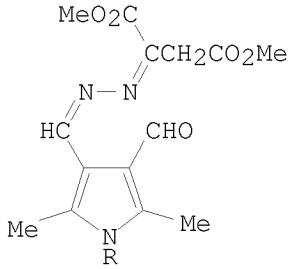
L6 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
TI Pyrrole studies. Part 32. A novel ring-cleavage reaction of the pyridazine ring during the reaction of 6H-pyrrolo[3,4-d]pyridazines with dimethyl acetylenedicarboxylate
GI



I



II



III

AB Treatment of pyrrolopyridazines I (R = Me, H, Ph) with (MeO2CC.tplbond.)2 in MeOH at -70° gave the corresponding esters II (R as before), which were unstable in the presence of H2O and underwent ring cleavage to

the corresponding pyrroles III. The structure of III (R = H) was confirmed by x-ray anal.

AN 1985:471267 CAPLUS <<LOGINID::20080623>>

DN 103:71267

OREF 103:11469a,11472a

TI Pyrrole studies. Part 32. A novel ring-cleavage reaction of the pyridazine ring during the reaction of 6H-pyrrolo[3,4-d]pyridazines with dimethyl acetylenedicarboxylate

AU Hernandez de la Figuera Gomez, Teresa; Sepulveda Arques, Jose; Jones, R. Alan; Dawes, Helen M.; Hursthouse, Michael B.

CS Dep. Quim. Org., Univ. Valencia, Valencia, Spain

SO Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (1985), (4), 899-902
CODEN: JCPRB4; ISSN: 0300-922X

DT Journal

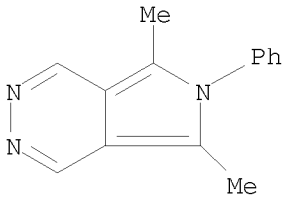
LA English

OS CASREACT 103:71267

IT 97476-49-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with di-Me acetylenedicarboxylate)

RN 97476-49-8 CAPLUS

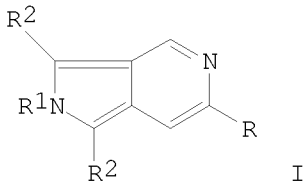
CN 6H-Pyrrolo[3,4-d]pyridazine, 5,7-dimethyl-6-phenyl- (CA INDEX NAME)



L6 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN

TI Structure and reactivity of iso-fused heterocyclic systems with 4n π and (4n + 2) π electrons. 8. Cyclizing condensation of 1H-pyrrole-3,4-dicarbaldehydes with 1,2-bifunctional compounds. A general and simple preparation method for 2H-pyrrolo[3,4-c]pyridines and 6H-pyrrolo[3,4-d]pyridazines

GI

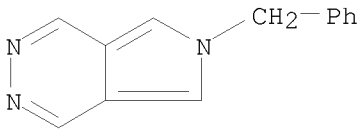


I

AB 2H-Pyrrolo[3,4-c]pyridines I (R = CO2Me, CO2Et, cyano; R1 = H, Me, CMe3, CH2Ph; R2 = H, Me) are easily and efficiently accessible via reaction of 1H-pyrrole-3,4-dicarbaldehydes with H2NCH2R.HCl. Under the influence of Et2NH the cyclocondensation occurs in an uniform fashion and in 55-99% yields. In a similar manner 1H-pyrrole-3,4-dicarbaldehydes react with N2H4; two-fold elimination of H2O leads to 6H-pyrrolo[3,4-d]pyridazines.

The bicyclic hetarenes are stabilized compared with 2H-isoindoles by addnl. heteroatoms in the 6-membered ring and acceptor groups at the 6-position.

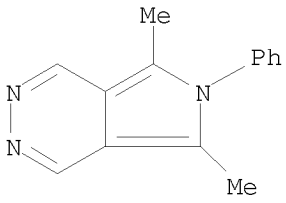
AN 1985:45802 CAPLUS <<LOGINID::20080623>>
DN 102:45802
OREF 102:7201a,7204a
TI Structure and reactivity of iso-fused heterocyclic systems with 4n π and (4n + 2) π electrons. 8. Cyclizing condensation of 1H-pyrrole-3,4-dicarbaldehydes with 1,2-bifunctional compounds. A general and simple preparation method for 2H-pyrrolo[3,4-c]pyridines and 6H-pyrrolo[3,4-d]pyridazines
AU Kreher, Richard P.; Pfister, Juergen
CS Abt. Chem., Univ. Dortmund, Dortmund, D-4600/50, Fed. Rep. Ger.
SO Chemiker-Zeitung (1984), 108(9), 275-7
CODEN: CMKZAT; ISSN: 0009-2894
DT Journal
LA German
OS CASREACT 102:45802
IT 94169-86-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 94169-86-5 CAPLUS
CN 6H-Pyrrolo[3,4-d]pyridazine, 6-(phenylmethyl)- (CA INDEX NAME)



L6 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
TI Aldehydes derived from 1,2,5-trisubstituted pyrroles
GI For diagram(s), see printed CA Issue.
AB cf. C.A. 50, 9413d. PhN.CR:CR1.CR2:CMe (I, R = Ph or Me, R1 = R2 = H) (II, III) formylated with HCONMe2 and POCl3, the corresponding aldehydes (I, R = Ph or Me, R1 = H, R2 = CHO) (IV, V) reduced, the trimethylpyrroles (I, R = Ph or Me, R1 = H, R2 = Me) (VI, VII) formylated and the aldehydes (I, R = Ph or Me, R1 = CHO, R2 = Me) (VIII, IX) again reduced yielded the completely substituted pyrroles (I, R = Ph or Me, R1 = R2 = Me) (X, XI). III also gave the dialdehyde (I, R = Me, R1 = R2 = CHO) (XII). Knorr-Paal condensation of PhNH2 with (AcCH2)2 and BzCH2CH2Ac, resp., purification of the condensation products by vacuum distillation and recrystn. (C6H12) gave II and III. III (25 g.) and 16 g. HCONMe2 in 100 ml. dry PhMe stirred well with portionwise addition of 27 g. POCl3 and the mixture heated 6 hrs. on a steam bath, shaken 20 min. with 300 ml. saturated aqueous NaOAc and extracted with PhMe, the washed (10% aqueous Na2CO3, H2O) and dried (Na2SO4) extract evaporated and the residue fractionated yielded 73% V, m. 92° (dilute MeOH), b12 190°; semicarbazone m. 294° (alc.). The residue from distillation recrystd. from alc. yielded 13% (with large excess of 3 moles HCONMe2) XII, m. 203°, giving a yellow halochromy with H2SO4. XII (1 g.) and 1 ml. N2H4.H2O refluxed 2 hrs. in alc. and the cooled mixture filtered gave 0.9 g. 1,3-dimethyl-2-phenyl-5,6-diazaisoindole, m. 288°, yellow coloration with H2SO4, an azine belonging to a group of compds. of biol. interest as potential antagonists of purine bases. XII (1 mole) treated with 2 moles PhCH2CN gave the bis(phenylacrylonitrile) derivative,

C30H23N3, m. 171° (alc.). V (8 g.) and 3 g. 95% N2H4.H2O heated 10 min. at 100° in 200 ml. (HOCH2CH2)2O and the mixture refluxed 90 min. with 3.9 g. KOH with removal of H2O, the cooled mixture acidified with dilute HCl and extracted with C6H6 yielded 86.6% VII, m. 39° (dilute MeOH), b18 140°. Similarly, 10 g. IV, 2.8 g. N2H4.H2O, and 3 g. KOH in 100 ml. (HOCH2CH2)2O yielded 87% VI, m. 79° (alc.), b12 195°, no halochromy with H2SO4. VII (11.5 g.), 6.8 g. HCONMe2, and 14.5 g. POCl3 in 100 ml. dry PhMe yielded 83.3% IX, m. 134° (MeOH); semicarbazone m. 273° (alc.). The same formylation technique applied to VI gave no aldehyde, even after heating 30 hrs. VI (5.5 g.) and 2.4 g. HCONMe2 treated portionwise with 4 g. POCl3 and the sticky violet mass heated 10 hrs. on a steam bath, the cooled mass treated with 15% aqueous NaOH and the product worked up yielded 77% VIII, m. 200° (C6H12), b17 254°; oxime m. 238-9°(alc.). VIII (6 g.), 1.4 g. N2H4.H2O, and 1.4 g. KOH in 50 ml. (HOCH2CH2)2O gave 4 g. X, m. 121° (C6H12 or AcOH). IX (5 g.), 1.7 g. N2H4.H2O and 2 g. KOH in (HOCH2CH2)2O yielded 70% XI, b12 142°, darkening rapidly on exposure to air and light, also obtained by reduction of XII. The aldehydes IV and V, with a free ortho position, reacted with PhCH2CN to give the corresponding acrylonitriles (XIII, XIV) whereas VIII and IX failed to react. V (1 mole) and 1 mole PhCH2CN in alc. refluxed 5 min. with a few drops of 5N NaOH and the cooled mixture diluted with H2O, filtered and the H2O-washed precipitate recrystd. (alc.)
gave 70% XIV, α-phenyl-β-(2,5-dimethyl-1-phenyl-3-pyrryl)acrylonitrile, m. 139°. The corresponding XIII, m. 145° (alc.), was similarly prepared from IV and PhCH2CN in alc.

AN 1960:50367 CAPLUS <<LOGINID::20080623>>
DN 54:50367
OREF 54:9884b-i
TI Aldehydes derived from 1,2,5-trisubstituted pyrroles
AU Rips, Richard; Buu-Hoi, Ng. Ph.
CS Univ. Paris
SO Journal of Organic Chemistry (1959), 24, 372-4
CODEN: JOCEAH; ISSN: 0022-3263
DT Journal
LA Unavailable
OS CASREACT 54:50367
IT 97476-49-8P, 6H-Pyrrolo[3,4-d]pyridazine, 5,7-dimethyl-6-phenyl-
RL: PREP (Preparation)
(preparation of)
RN 97476-49-8 CAPLUS
CN 6H-Pyrrolo[3,4-d]pyridazine, 5,7-dimethyl-6-phenyl- (CA INDEX NAME)



L6 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
TI Friedel-Crafts acylations of 1-phenyl-2,5-dimethylpyrrole and 1,2-diphenyl-5-methylpyrrole
AB Friedel-Crafts acylations of 1-phenyl-2,5-dimethyl-pyrrole (I) yield diketones when acetyl (II) and propionyl chlorides (III) are used, and both mono- and diketones with BzCl (IV) and anisoyl chloride (V). On the

other hand, 1,2-diphenyl-5-methylpyrrole (VI) gave predominantly monoketones with both type of acid chlorides, substitution occurring at the 4-position. Condensation of 3,4-diacylpyrroles with $N_2H_4.H_2O$ led to derivs. of 5,6-diazaisoindole, a new heterocyclic nucleus analogous to purine. I (15 g.) and 14 g. $AlCl_3$ in 200 ml. CS_2 treated with 7.5 g. II portionwise, the mixture heated 2 hrs. at 40°, cooled, H_2O added, washed with 5% aqueous NaOH, dried, and distilled gave 9 g. 3,4-diacetyl-1-phenyl-3,5-dimethylpyrrole (VII), b15 235-40°, prisms, m. 98°, yellow color with H_2SO_4. In an experiment in which $AlCl_3$ was added at 0°, and the mixture kept overnight at 15°, an 18% yield VII was obtained. I (20 g.) and 10 g. II in 100 ml. dry thiophene-free C_6H_6 heated 2 hrs. at 50° with 36.5 g. $SnCl_4$ gave 52% VII. VII (2.5 g.) in 10 ml. alc. was treated with 1 g. 95% $N_2H_4.H_2O$; an exothermic reaction occurred, and a precipitate was collected to give 2.2. g. 1,3,4,7-tetramethyl-2-phenyl-5,6-diazaisoindole, m. 318° (MeOH), yellow color with H_2SO_4. I (10 g.) and 12 g. III in 100 ml. C_6H_6 treated with 18.2 g. $SnCl_4$ gave 14 g. of the dione (VIII), b20 252°, silky needles, m. 66°. VIII was obtained in 25% yield when $AlCl_3$ was used as catalyst, the reaction being performed at room temperature and in CS_2. VIII (1.4 g.) and 0.5 g. $N_2H_4.H_2O$ in 5 ml. alc. refluxed 3 hrs. gave 1,3-dimethyl-2-phenyl-4,7-diethyl-5,6-diazaisoindole, m. 190° (aqueous MeOH). I (20 g.), 18 g. BzCl, and 37 g. $SnCl_2$ in C_6H_6 gave 2 ketonic portions. The lower-boiling portion of 15 g. consisted of 3-benzoyl-1-phenyl-2,5-dimethylpyrrole, b15 260°, leaflets, m. 126°. The higher-boiling fraction of 10 g. consisted of 3,4-dibenzoyl-1-phenyl-2,5-dimethylpyrrole (IX), b17 320-30°, plates, m. 186°. A similar reaction, using the same amts. of starting materials, and performed with $AlCl_3$ at 40° in CS_2 gave 17 g. IX. IX (0.5 g.) and 0.4 g. $N_2H_4.H_2O$ in 5 ml. alc. gave 0.4 g. 1,3-dimethyl-1,4,7-triphenyl-5,6-diazaisoindole, yellow needles, m. 294°(alc.). I (20 g.), 22 g. V, and 16.5 g. $AlCl_3$ at 40° in CS_2 gave 2 portions, one of 5.5 g. of 3-anisoyl-1-phenyl-2,5-dimethylpyrrole (X), lustrous leaflets, m. 116°, b14 275-90°. The other portion of 15 g. consisted of 3,4-dianisoyl-1-phenyl-2,5-dimethylpyrrole (XI), b2 300°, leaflets, m. 183°. A $SnCl_4$-catalyzed acylation using the same amts. of starting materials gave 10 g. X and 10 g. XI. 1,3-Dimethyl-1-phenyl-4,7-bis(p-methoxyphenyl)-5,6-diazaisoindole crystallized as lemon-yellow plates, m. 295°(alc.). All the acylations of VI were effected with equimolar amts. of VI and of the acid chlorides. The acetylation, performed at various temps. and with $AlCl_3$ as well as $SnCl_2$, gave predominantly 4-acetyl-1,2-diphenyl-5-methylpyrrole (XII), b11, 240-2°, needles, m. 101-2°; oxime, prisms, m. 176° (alc.). Repeated fractional crystallization from MeOH of the higher-boiling fractions gave small amts. of 3,4-diacetyl-1,2-diphenyl-5-methylpyrrole (XIII), m. 161°, yellow coloration with H_2SO_4. The yields of XII and XIII are recorded as follows (catalyst, temperature of reaction, and % total yield of XII and XIII given): $AlCl_3$, 0-5°, 15; $AlCl_3$, 18°, 38; $AlCl_3$, 40°, 52; $SnCl_4$, 18°, 48; $SnCl_4$, 60°, 59. 1,2-Diphenyl-3,4,7-trimethyl-5,6-diazaisoindole crystallized as silky needles, m. 239° (aqueous alc.). VI propionylated 3 hrs. at 50° with $SnCl_4$ gave 60% 4-propionyl-1,2-diphenyl-5-methyl-pyrrole (XIV), b15 254-5°, leaflets, m. 126° (alc.). No dione could be isolated from the higher-boiling fractions. With $AlCl_3$ as catalyst at 40°, a 40% yield of XIV was obtained; semicarbazone, leaflets, m. 260° (alc.). VI with IV and $SnCl_4$ at 50° gave 2 products; 49% 4-benzoyl-1,2-diphenyl-5-methylpyrrole, b0.3 244°, prisms, m. 131-2° (MeOH); 2,4-dinitrophenylhydrazone, prisms, m. 190° (aqueous dioxane). A 32% yield of 3,4-dibenzoyl-1,2-diphenyl-5-methylpyrrole (XV) was obtained, b0.5 above 260°, prisms, m. 200° (alc.).

With AlCl3 at 40°, a 39 % yield of XV was recorded. 1,2,4,7-Tetraphenyl-3-methyl-5,6-diazaisoindole crystallized from alc. as lemon-yellow plates, m. 277°, golden-yellow color in H2SO4. VI with SnCl4 and V at 50° gave 51% 4-anisoyl-1,2-diphenyl-5-methylpyrrole, b11 310-12°, prisms, m. 179-80° (alc.) [semicarbazone, m. 241° (alc.)], and 40% yield 3,4-dianisoyl-1,2-diphenyl-5-methylpyrrole (XVI), b0.5 300-5° (alc.), prisms, m. 208°. With AlCl3 a 29% yield of XVI was obtained at 40°, and a 9% yield when the reaction was performed at room temperature 1,2-Diphenyl-3-methyl-4,7-bis(p-methoxyphenyl)-5,6-diazaisoindole obtained as yellow plates, m. 301° (alc.), deep yellow color with H2SO4. The above listed diazaisoindoles may have biol. interest as potential antipurines.

AN 1959:122015 CAPLUS <<LOGINID::20080623>>
DN 53:122015
OREF 53:21878b-i,21879a-c
TI Friedel-Crafts acylations of 1-phenyl-2,5-dimethylpyrrole and 1,2-diphenyl-5-methylpyrrole
AU Rips, Richard; Buu-Hoi, Ng. Ph.
CS Univ. Paris
SO Journal of Organic Chemistry (1959), 24, 551-4
CODEN: JOCEAH; ISSN: 0022-3263
DT Journal
LA Unavailable
OS CASREACT 53:122015
IT 109450-25-1P, 6H-Pyrrolo[3,4-d]pyridazine, 1,4,5,7-tetramethyl-6-phenyl- 109562-64-3P, 6H-Pyrrolo[3,4-d]pyridazine, 1,4-diethyl-5,7-dimethyl-6-phenyl-
RL: PREP (Preparation)
(preparation of)
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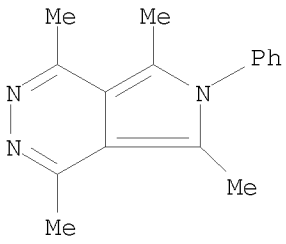

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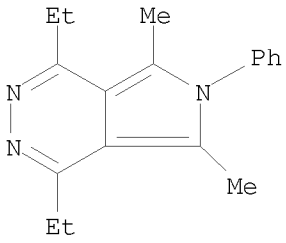

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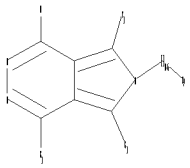

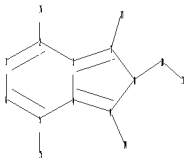

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10-11

G1:H,C

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
11:Atom 14:CLASS 15:CLASS 16:CLASS 17:CLASS

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FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 7970 TO 10550
PROJECTED ANSWERS: 21 TO 417

L8 11 SEA SSS SAM L7

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L8 11 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN 6H-Pyrrolo[3,4-d]pyridazin-1-amine, 6-(4-ethoxyphenyl)-4,5,7-trimethyl-N-[2-(1-pyrrolidinyl)ethyl]-
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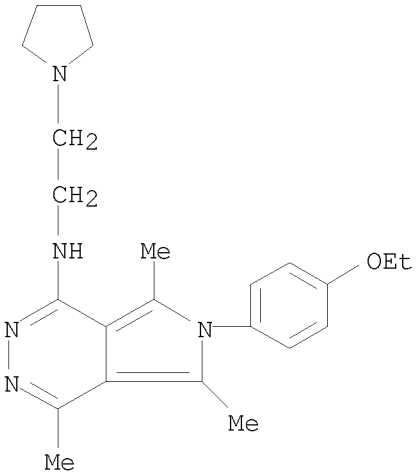

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HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):3

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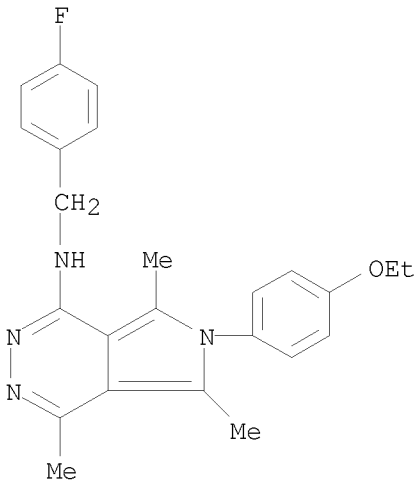
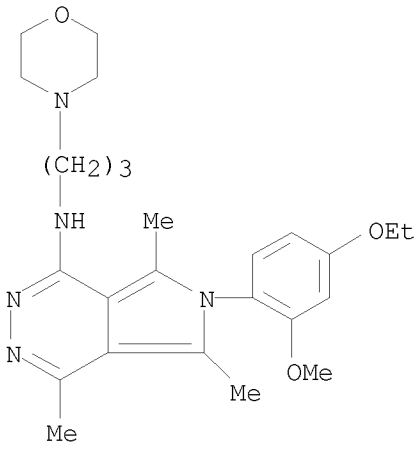
MF C24 H25 F N4 O



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L8 11 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN 6H-Pyrrolo[3,4-d]pyridazin-1-amine, 6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-N-[3-(4-morpholinyl)propyl]-
MF C25 H35 N5 O3



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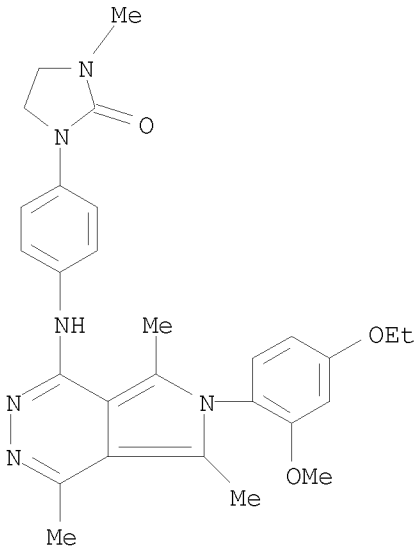
L8 11 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN 2-Imidazolidinone, 1-[4-[[6-(4-ethoxy-2-methoxyphenyl)-4,5,7-trimethyl-6H-pyrrolo[3,4-d]pyridazin-1-yl]amino]phenyl]-3-methyl-
MF C28 H32 N6 O3



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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	178.36	418.74

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-8.80

FILE 'CAPLUS' ENTERED AT 17:08:36 ON 23 JUN 2008

FILE COVERS 1907 - 23 Jun 2008 VOL 148 ISS 26
FILE LAST UPDATED: 22 Jun 2008 (20080622/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/legal/infopolicy.html

=> s l9
L10   3 L9

=> d l10 1-3 ti abs bib hitstr

L10 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN
TI   Expedited SAR study of high-affinity ligands to the α2δ
     subunit of voltage-gated calcium channels: Generation of a focused library
     using a solution-phase Sn2Ar coupling methodology
AB   The SAR of the lead compound 3, a novel ligand for the α2δ
     subunit of voltage-gated calcium channels, was rapidly explored.
     Utilizing a parallel solution-phase Sn2Ar coupling approach, a focused
     library was obtained. The library was evaluated in vitro and afforded a
     series of analogs with improved potencies. The SAR trends of the library
     are also described.
AN   2005:1342000 CAPLUS <<LOGINID::20080623>>
DN   144:100381
TI   Expedited SAR study of high-affinity ligands to the α2δ
     subunit of voltage-gated calcium channels: Generation of a focused library
     using a solution-phase Sn2Ar coupling methodology
AU   Chen, Chixu; Stearns, Brian; Hu, Tao; Anker, Naomi; Santini, Angelina;
     Arruda, Jeannie M.; Campbell, Brian T.; Datta, Purabi; Aiyar, Jayashree;
     Munoz, Benitio
CS   Department of Chemistry, Merck Research Laboratories, San Diego, CA,
     92121, USA
SO   Bioorganic & Medicinal Chemistry Letters (2006), 16(3), 746-749
     CODEN: BMCLE8; ISSN: 0960-894X
PB   Elsevier B.V.
DT   Journal
LA   English
OS   CASREACT 144:100381
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     647847-49-2P 647847-52-7P 647847-55-0P
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     647847-74-3P 647847-75-4P 647847-76-5P
     647847-88-9P 647848-14-4P 647848-17-7P
     647848-45-1P 647848-50-8P 647848-55-3P
     647848-57-5P 647848-62-2P 647848-68-8P
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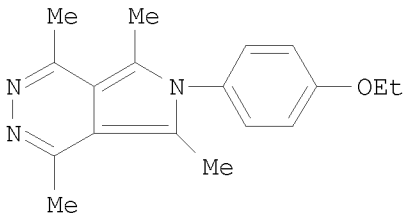
     RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); THU
     (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study);
     PREP (Preparation); USES (Uses)
        (SAR of high-affinity ligands to α2δ subunit of
        voltage-gated calcium channels: generation of focused library using
        solution-phase Sn2Ar coupling methodol.)
RN   647846-36-4 CAPLUS
CN   6H-Pyrrolo[3,4-d]pyridazin-1-amine, 6-(4-ethoxyphenyl)-N-1H-indol-5-yl-
     4,5,7-trimethyl- (CA INDEX NAME)

L10 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN

TI Synthesis and biological evaluation of 6-aryl-6H-pyrrolo[3,4-d]pyridazine derivatives: high-affinity ligands to the α2δ subunit of voltage gated calcium channels

GI



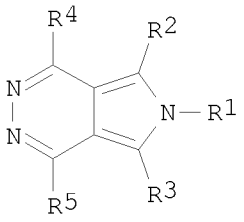
I

AB A novel class of 6-aryl-6H-pyrrolo[3,4-d]pyridazine ligands for the α2δ subunit of voltage-gated calcium channels has been described. Substitutions in the aryl ring of the mol. were generally not tolerated, and resulted in diminished binding to the α2δ subunit. Modifications to the pyridazine ring revealed numerous permissive substitutions, and detailed SAR studies were carried out in this portion of the mol. Replacement of the pyridazine ring Me group with an aminomethyl functionality provided greatly improved potency over the initial lead. The initial lead compound (I) displayed good rat pharmacokinetic properties, and was shown to be efficacious in the Chung model for neuropathic pain in rats.

AN 2004:153601 CAPLUS <<LOGINID::20080623>>
DN 140:357282
TI Synthesis and biological evaluation of 6-aryl-6H-pyrrolo[3,4-d]pyridazine derivatives: high-affinity ligands to the α2δ subunit of voltage gated calcium channels
AU Stearns, Brian A.; Anker, Naomi; Arruda, Jeannie M.; Campbell, Brian T.; Chen, Chixu; Cramer, Merryl; Hu, Tao; Jiang, Xiaohui; Park, Kenneth; Ren, Kun Kun; Sablad, Marciano; Santini, Angelina; Schaffhauser, Herve; Urban, Mark O.; Munoz, Benito
CS Department of Medicinal Chemistry, Merck Research Laboratories, San Diego, CA, 92121, USA
SO Bioorganic & Medicinal Chemistry Letters (2004), 14(5), 1295-1298
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science B.V.
DT Journal
LA English
OS CASREACT 140:357282
IT 647845-93-0P 647845-94-1P 647845-96-3P
647845-97-4P 647845-98-5P 682359-68-8P
682359-69-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of 6-aryl-6H-pyrrolo[3,4-d]pyridazine derivs. as high-affinity ligands to the α2δ subunit of voltage gated calcium channels)
RN 647845-93-0 CAPLUS
CN 6H-Pyrrolo[3,4-d]pyridazin-1-amine, 6-(4-ethoxyphenyl)-N,4,5,7-tetramethyl- (CA INDEX NAME)

L10 ANSWER 3 OF 3 CAPLUS

TI Treatment of neuropathic pain with 6H-pyrrolo[3,4-d]pyridazine compounds
GI



I

AB The title compds. [I; R1 = (un)substituted alkyl(hetero)aryl, alkyl(hetero)cycloalkyl, (hetero)aryl, (hetero)cycloalkyl; R2-R5 = a bond, (un)substituted alkyl, alkyl(hetero)aryl, alkyl(hetero)cycloalkyl, (hetero)aryl, (hetero)cycloalkyl] were prepared as as ligands of voltage gated calcium channels (VGCC), useful in the treatment of neuropathic pain, and psychiatric and mood disorders such as, for example, schizophrenia, anxiety, depression, panic, and bipolar disorder, as well as in the treatment of pain, Parkinson s disease, cognitive dysfunction, epilepsy, circadian rhythm disorders, drug addiction, drug abuse, drug withdrawal and other. E.g., a multi-step synthesis of I [R1 = 4-EtOC6H4; R2-R4 = Me; R5 = 4-MeOC6H4] which produced a 65% effect after i.p. dosing at 30 mg/kg in spinal nerve ligation model of neuropathic pain in rats, was given. The pharmaceutical composition comprising the compound I is claimed.

AN 2004:60243 CAPLUS <<LOGINID::20080623>>
DN 140:111422
TI Treatment of neuropathic pain with 6H-pyrrolo[3,4-d]pyridazine compounds
IN Anker, Naomi Burke; Arruda, Jeannie M.; Campbell, Brian Thomas; Munoz, Benito; Prasit, Petpiboon; Stearns, Brian A.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 203 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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